REMARKS

The present invention relates in part to the use of affinity tags in recombinant fusion protein constructs. In particular, the claimed invention relates to affinity tags which comprise two or more modules capable of mediating binding to streptavidin.

Prior to the present submission, claims 1–34, 36, 37, 40–45 and 47 were pending in the application, with claims 16, 17, 32–34, 36, 37, 40–45, and 47 under examination. The balance of the claims have been withdrawn from examination by the Examiner in accordance with a restriction requirement.

Claims 16, 17, 36, 37, 41–45, and 47 have been amended, claim 40 has been cancelled, and new claims 48–51 added by the present submission. Support for the recitation of at least one streptavidin module comprising a sequence –His–Pro–Gln–Phe– may be found in the specification, for example at page 14, lines 14–23, in original claim 10, and in the sequence listing. The remaining claim amendments are made solely to clarify the claimed subject matter, and do not change the scope of the claims. Support for new claims 48-51 may be found in the specification at page 8, lines 13-16; and page 13, lines 14-20.

Reconsideration of the claimed invention is respectfully requested in view of the foregoing amendments and the remarks contained herein.

I. Rejection Under 35 U.S.C. §112, First Paragraph

The rejection of the pending claims as allegedly not satisfying the written description requirement is respectfully traversed.

The claimed invention relates to provision of a fusion protein comprising a streptavidin–binding peptide linked to a protein sequence of interest. As recited in claim 16, the streptavidin–binding peptide comprises a sequential arrangement of two modules with an amino acid sequence of –His–Pro–Baa– in which Baa is selected from the group consisting of glutamine, asparagine and methionine. At least one of the modules comprises a sequence –His–Pro–Gln–Phe–. The streptavidin–binding peptide is located at the carboxy terminal end or at the amino terminal end of the protein sequence to which it is fused.

The Office Action asserts on page 3 that "there is no description provided of a particular protein to know what the fusion protein will look like." This is incorrect. The claims provide all relevant information regarding the fusion protein. This fusion protein has located at the amino

and/or carboxyl terminus of a protein sequence of interest a streptavidin–binding peptide, and a specific sequence is called out for the streptavidin binding portion of the streptavidin–binding peptide.

As far as the remainder of the fusion protein structure, the skilled artisan is well versed in the use of affinity tags as part of a fusion protein. The skilled artisan has been aware of the use of affinity tags at the C- and N-terminus of recombinant proteins for more than two decades. See, for example, European Patent Application 0 282 042 published September 14, 1988, which corresponds to US patent 5,310,663 the content of which was discussed in applicant's reply dated November 1, 2007. The present invention provides a description of new affinity tags. As Applicant has noted previously, the remainder of the fusion protein structure – that is, the polypeptide sequence of interest to which the affinity tag is linked – is not a relevant consideration to one skilled in the art.

The binding characteristics of the fusion protein to streptavidin are determined by the structure of the affinity tag, not the polypeptide sequence of interest to which the affinity tag is linked. The Office Action does not explain why one skilled in the art would somehow believe that the affinity tags described in the present specification would not work in the same manner as those previously known in the art. Further, the criticism on page 3 of the Office Action that "the claims are directed to a streptavidin binding peptide linked to any unknown protein" and so "a skilled artisan cannot envision the detailed chemical structure of the fusion protein" can only be made from the point of view of one lacking the requisite knowledge of the art.

The proper standard for determining compliance with the written description requirement of 35 U.S.C. § 112, first paragraph, is whether the specification reasonably conveys to the skilled artisan that the inventor was in possession of the claimed invention as of the filing date. See MPEP § 2163.02 (citing Ralston Purina Co. v. Far-Mar-Co., Inc., 227 USPQ 177, 179 (Fed. Cir. 1985)). An adequate written description "may be shown by any description of sufficient, relevant, identifying characteristics so long as a person skilled in the art would recognize that the inventor had possession of the claimed invention." MPEP § 2163(II)(3)(a).

Applicant respectfully submits that the specification reasonably conveys to the skilled artisan that the inventor was in possession of the claimed invention as of the filing date. Because the written description requirement demands no more, Applicant requests that the rejection be reconsidered and withdrawn.

II. Rejection Under 35 U.S.C. §112, First Paragraph

The rejection of the pending claims as allegedly not satisfying the enablement requirement is respectfully traversed.

Like the rejection premised on the Written Description requirement, the Enablement rejection presented in the Office Action continues to focus on characteristics of the claimed fusion proteins which are irrelevant from the point of view of one skilled in the art.

The Office Action is focused on the overall structure of the fusion protein, as if the ability to bind to streptavidin is somehow conveyed by the complete protein sequence. This is not the case. As noted above, the skilled artisan has been aware of the use of affinity tags at the C- and N-terminus of recombinant proteins for more than two decades. Once again, Applicant notes that the binding characteristics of the fusion protein to streptavidin are determined by the structure of the affinity tag, not by the polypeptide sequence of interest to which the affinity tag is linked. And the structure of the affinity tag is plainly and unambigouously recited in the claim.

In contrast, the statements in the Office Action to the effect that "no structure is provided for said fusion protein to make the correlation between structure and function" (Office Action, page 5), and "[a] skilled artisan cannot predict that any known or unknown protein would bind to streptavidin" (Office Action, page 6) appear to be made from the point of view of one who has no experience in the use of such affinity tags. Indeed, the entirety of the rejection continues in this vein, alleging that various "changes" or "mutations" can affect the function of a protein, and that this allegedly introduces "unpredictability" into the invention.

None of this discussion in the Office Action appears to understand and acknowledge the routine use of such affinity tags in the art for more than two decades. And nothing in the Office Action explains why one skilled in the art would expect the present affinity tags to differ in their usefulness from all other affinity tags previously known in the art.

It is well established in the patent law that a specification is presumed to be enabling. Also, as stated in MPEP § 2164.04, "it is incumbent on the Patent Office… to explain why it doubts any statement in a disclosure, and to back up its assertions of its own with acceptable evidence or reasoning…. Otherwise, there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure." Instead of providing such evidence or reasoning, the Office Action ignores the extensive knowledge available in the art

concerning affinity tags generally and the teachings of the specification concerning the claimed affinity tag structures.

Applicant respectfully submits that, when a proper enablement standard is applied, it is apparent that one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation. Because the enablement requirement demands no more, Applicant respectfully requests that the rejection be reconsidered and withdrawn.

III. REJECTION UNDER 35 U.S.C. §102(e)

The rejection of claims 16, 17, 40, and 41 under 35 U.S.C. §102(e) as allegedly being anticipated by Skerra *et al.*, U.S. Patent No. 5,506,121 is respectfully traversed.

The claimed invention relates to provision of a fusion protein comprising a streptavidin–binding peptide linked to a protein sequence of interest. As recited in claim 16, the streptavidin–binding peptide comprises a sequential arrangement of two modules with an amino acid sequence of –His–Pro–Baa– in which Baa is selected from the group consisting of glutamine, asparagine and methionine. At least one of the modules comprises a sequence –His–Pro–Gln–Phe–.

By contrast, the '121 patent discloses the use of a single peptide having the sequence Trp–X–His–Pro–Gln–Phe–Y-Z as an affinity tag. The Examiner does not assert that the '121 patent discloses the claimed sequential arrangement of two modules.

In order to establish a *prima facie* case of anticipation, the Examiner bears the burden of demonstrating that each and every limitation of the claimed methods is present in the cited reference. In this case, the Examiner has not bet that burden. Because no prima facie case of anticipation has been established, Applicant requests that the rejection be reconsidered and withdrawn.

IV. REJECTION UNDER 35 U.S.C. §102(e)

The rejection of claims 16, 17, 32, 40, and 41 under 35 U.S.C. §102(e) as allegedly being anticipated by Szostak *et al.*, U.S. Patent No. 6,841,359 is respectfully traversed.

The claimed invention relates to provision of a fusion protein comprising a streptavidin–binding peptide linked to a protein sequence of interest. As recited in claim 16, the streptavidin–

binding peptide comprises a sequential arrangement of two modules with an amino acid sequence of –His–Pro–Baa– in which Baa is selected from the group consisting of glutamine, asparagine and methionine. At least one of the modules comprises a sequence –His–Pro–Gln–Phe–.

By contrast, the '359 patent fails to disclose the use of a module comprising a sequence –His–Pro–Gln–Phe–.

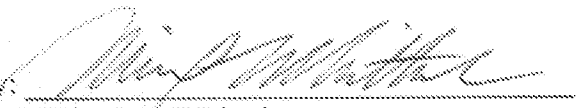
In order to establish a *prima facie* case of anticipation, the Examiner bears the burden of demonstrating that each and every limitation of the claimed methods is present in the cited reference. In this case, the Examiner has not bet that burden. Because no prima facie case of anticipation has been established, Applicant requests that the rejection be reconsidered and withdrawn.

CONCLUSION

For the reasons set forth herein, Applicant respectfully submits that claims 16, 17, 32–34, 36, 37, 41–45, and 47-51 are in condition for allowance. Applicants respectfully request that the Examiner reconsider and withdraw the grounds for rejection set forth in the Office Action.

If the Examiner would like to discuss any of the issues raised in the Office Action, Applicant's representative can be reached at (619) 203-3186.

Respectfully submitted,

By: 

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Date: August 26, 2008

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